II. REMARKS

Claims 1-33 are pending and stand variously rejected under 35 U.S.C. §§ 102 and 103. Claims 1, 2 and 10 have been amended in a sincere effort to advance prosecution. In particular, claims 1 and 10 have been amended to specify that the information obtained from the electronic image now includes specified biochemical components, as described for example on page 46, lines 25-26 of the specification. Claim 2 has been amended to correct a typographical error in sub-section (7). The specification has also been amended to correct typographical errors in various descriptions of the Figures. No new matter has been added as a result of these amendments and entry thereof is respectfully requested.

In view of the foregoing amendments and following remarks, Applicants respectfully requested reconsideration of the application.

35 U.S.C. § 102

Claim 1 stands rejected as allegedly anticipated under 35 U.S.C. § 102(e) by U.S. Patent No. 6,334,006 (hereinafter "Rupprecht"). In support of these rejections, it is alleged that Rupprecht teaches treating a human with a joint disease. (Office Action, page 2).

Applicants traverse on the grounds that Rupprecht is not a proper 102(e) reference. In particular, Rupprecht's earliest priority date is December 21, 1999. The application at issue claims the benefit of a PCT application filed December 16, 1999. Accordingly, Rupprecht is not a proper reference against the pending application and Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. § 103(a)

Claims 1-33 stand rejected as allegedly obvious over U.S. Patent No. 5,320,102 (hereinafter "Paul") in view of U.S. Patent No. 5,853,746 (hereinafter "Hunziker"). In support of this rejection the Office Action states:

> Paul teaches a method of diagnosing cartilage disease, comprising MR imaging of the cartilages at different times (column 3, lines 58-67), analyzing the images by looking at cartilage thickness and biochemical constituents, such as the proteoglycan levels (column 4, lines 20-25 and column 5, lines 65-67), determining whether a joint is diseased by looking at the proteoglycan levels, and selecting a particular therapy based on the diagnosis. (column 11, lines 35-55). However, Paul fails to teach a particular therapy. Hunziker teaches a method of

> cartilage therapy comprising the use of growth factors. (column 19, lines 25-67 and column 24, lines 55-60). It would have been obvious to one having ordinary skill in the art at the time the invention was made to adapt the teachings of Hunziker to that of Paul such that proper treatment could be made to cure the diseased cartilage. (Office Action, page 3).

Applicants traverse the rejection and supporting remarks.

The Office bears the burden of establishing a *prima facie* case of obviousness. *See, e.g., In re Ryckaert,* 28 USPQ2d 1955, 1956 (Fed. Cir. 1993); and *In re Oetiker,* 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). In order to establish a *prima facie* case of obviousness, the cited references must teach or suggest all the limitations of the claims. *See, In re Wilson,* 165 USPQ 494, 496 (CCPA 1970). The Federal Circuit has repeatedly held that using "hindsight reconstruction" to provide the necessary motivation is improper. (see, e.g., *In re Fine,* 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) and *In re Napier* 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) stating that "obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention absent some teaching, suggestion or incentive supporting the combination."). Further, common knowledge and common sense are not the specialized knowledge and expertise necessary to establish a motivation to arrive at the claimed invention. See, *e.g., In re Lee,* 61 USPQ2d 1430 (Fed. Cir. 2002).

The combination of references cited by the Office does not teach or suggest all the elements of the rejected claims. Paul is directed entirely toward diagnosing proteoglycan deficiency in cartilage by quantifying pixel intensity of a two-dimensional MRI. In contrast, pending claims 1 through 22 are drawn to methods of treating joint disease using information obtained from an electronic image where the information does not include information regarding proteoglycan content. Pending claims 23 through 33 are directed to methods of treating a human with diseased cartilage in a joint using an MRI image to create a 3D geometric model. Nowhere does Paul teach or suggest such 3D MRI imaging techniques or the generation of geometric models. For its part, Hunziker fails entirely to teach or suggest evaluating electronic images to select a therapy for diseased cartilage. Thus, Paul and Hunziker fail to teach or suggest elements of the pending claims.

In sum, the obviousness rejection is improper because the references do not teach or suggest the elements of the claims and because there is no motivation to combine their teachings

as set forth by the Office. Accordingly, Applicants respectfully request that the rejection withdrawn.

III. CONCLUSION

In view of the foregoing remarks, Applicants submit that the pending claims are sufficiently definite and define an invention that is described, enabled and patentable over the art of record. Accordingly, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

Should the Examiner have any further questions, Applicants request that the undersigned be contacted at (650) 325-7812.

Respectfully submitted,

Date: 23 Dec 02

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Version Showing Changes Made to Specification

The paragraph beginning on line 1 of page 18 has been amended as follows:

--Figures 8A and 8B show a 3-point Dixon GRE image of the articular cartilage of medial femorotibial compartment in a normal 35-year old volunteer. Figure ~~13A~~ 8A has the subject in a supine position and Figure ~~13B~~ 8B has the subject in an upright position.--

The paragraph beginning on line 8 of page 18 has been amended as follows:

--Figure ~~9B~~ 11B is a 2D cartilage thickness map demonstrating abrupt decrease in cartilage thickness in an area of the defect (arrows). The Δ thickness between the neighboring pixels can be [use] used to define the borders of the cartilage defect. Note ~~defused~~ diffuse cartilage thinning in the area enclosed by the asterisks (*).--

The paragraph beginning on line 11 of page 18 has been amended as follows:

--Figures 10A-10C show a 3D surface registration of femoral condyles based on T1-weighted ~~Spin-Echo~~ spin-echo MR images. Figure ~~6A~~ 10A is baseline with a knee [and] in neutral position. Figure ~~6B~~ 10B is a follow-up with knee and external rotation with a 3D view that is the identical to the one used in ~~6A~~ 10A but the difference in knee rotation is apparent. In Figure ~~6C~~ 10C, transformation and re-registration of Scan B~~in~~ to the object coordinate system of Scan A shows the anatomic match to A is excellent.--

Version Showing Changes Made to Claims

1. (Amended) A method of treating a human joint disease involving cartilage, which method comprises:

obtaining an electronic image of said joint, wherein said image includes both normal and diseased cartilage tissue;

electronically evaluating said image to obtain information [comprising] selected from the group consisting of volume, area, thickness, curvature, geometry, [biochemical contents,] water content, sodium content, hyaluronic acid content, signal intensity or relaxation time of said normal or diseased tissue; and

selecting a therapy based on said information.

2. (Amended) The method of claim 1, wherein said electronically evaluating comprises a method selected from the group consisting of (1) a method of estimating the loss of cartilage in a joint, wherein the joint comprises cartilage and accompanying bones on either side of the joint, which method comprises obtaining a three-dimensional map of the cartilage at an initial time and calculating the thickness or regional volume of a region of degenerated cartilage so mapped at the initial time, obtaining a three-dimensional map of the cartilage at a later time, and calculating the thickness or regional volume of a region of degenerated cartilage so mapped at the later time, and determining the loss in thickness or regional volume of the region of degenerated cartilage between the later and initial times; (2) a method for assessing the condition of cartilage in a joint of a human, which method comprises electronically transferring an electronically generated image of a cartilage of the joint from a transferring device to a receiving device located distant from the transferring device; receiving the transferred image at the distant location; converting the transferred image to a degeneration pattern of the cartilage; and transmitting the degeneration pattern to a site for analysis; (3) a method for determining the volume of cartilage loss in a region of a cartilage defect of a cartilage in a joint of a mammal which method comprises determining the thickness, D_N, of the normal cartilage near the cartilage defect; obtaining the thickness of the cartilage defect, D_D, of the region; subtracting D_D from D_N to give the thickness of the cartilage loss, D_L; and multiplying the D_L value times the area of the cartilage defect, A_D, to give the volume of cartilage loss; (4) a method of estimating the change of cartilage in a joint of a mammal over

time, which method comprises estimating the thickness or width or area or volume of a region of cartilage at an initial time T_1; estimating the thickness or width or area or volume of the region of cartilage at a later time T_2; and determining the change in the thickness or width or area or volume of the region of cartilage between the initial and the later times; (5) a method for providing a biochemically based map of joint cartilage of a mammal, wherein the joint comprises cartilage and associated bones on either side of the joint, which method comprises measuring a detectable biochemical component throughout the cartilage; determining the relative amounts of the biochemical component throughout the cartilage; mapping the amounts of the biochemical component in three dimensions through the cartilage; and determining the areas of abnormally joint cartilage by identifying the areas having altered amounts of the biochemical component present; (6) a method of estimating the change of cartilage in a joint, wherein the joint comprises articular cartilage, which method comprises defining a 3D object coordinate system of the joint at an initial time, T_1; identifying a region of a cartilage defect within the 3D object coordinate system; defining a volume of interest around the region of the cartilage defect whereby the volume of interest is larger than the region of cartilage defect, but does not encompass the entire articular cartilage; defining the 3D object coordinate system of the joint at a second timepoint, T_2; placing the identically-sized volume of interest into the 3D object coordinate system at timepoint T_2 using the object coordinates of the volume of interest at timepoint T_1; and measuring any differences in cartilage volume within the volume of interest between timepoints T_1 and T_2; and (7) a method for correlating cartilage image data, bone image data, and optoelectrical image data for the assessment of the condition of a joint, which method comprises (a) obtaining the cartilage image data of the joint with a set of skin reference markers placed externally near the joint; (b) obtaining the bone image data of the joint with a set of skin reference markers positioned in the same manner as the markers in (a); (c) obtaining the optoelectrical image data of the joint with a set of skin reference markers positioned in the same manner as (a) and (b); and using the skin reference markers to correlate the images obtained in (a), (b) and (c) with each other, wherein each skin reference marker is detectable in the cartilage and bone data and the opto-electrical data.

10. (Amended) A method of treating cartilage degeneration in a joint, which method comprises:

obtaining an electronic image of said joint, wherein said image includes both normal and diseased cartilage tissue;

electronically evaluating said image to obtain information [comprising] selected from the group consisting of volume, area, thickness, geometry, [biochemical contents,] water content, sodium content, hyaluronic acid content or relaxation time of said normal or diseased tissue; and

selecting a therapy to treat or replace said degenerated cartilage, wherein said information is used during selection of treatment or replacement therapy of said degenerated cartilage.

Currently Pending Claim Set

1. (Amended) A method of treating a human joint disease involving cartilage, which method comprises:

obtaining an electronic image of said joint, wherein said image includes both normal and diseased cartilage tissue;

electronically evaluating said image to obtain information selected from the group consisting of volume, area, thickness, curvature, geometry, water content, sodium content, hyaluronic acid content, signal intensity or relaxation time of said normal or diseased tissue; and

selecting a therapy based on said information.

2. (Amended) The method of claim 1, wherein said electronically evaluating comprises a method selected from the group consisting of (1) a method of estimating the loss of cartilage in a joint, wherein the joint comprises cartilage and accompanying bones on either side of the joint, which method comprises obtaining a three-dimensional map of the cartilage at an initial time and calculating the thickness or regional volume of a region of degenerated cartilage so mapped at the initial time, obtaining a three-dimensional map of the cartilage at a later time, and calculating the thickness or regional volume of a region of degenerated cartilage so mapped at the later time, and determining the loss in thickness or regional volume of the region of degenerated cartilage between the later and initial times; (2) a method for assessing the condition of cartilage in a joint of a human, which method comprises electronically transferring an electronically generated image of a cartilage of the joint from a transferring device to a receiving device located distant from the transferring device; receiving the transferred image at the distant location; converting the transferred image to a degeneration pattern of the cartilage; and transmitting the degeneration pattern to a site for analysis; (3) a method for determining the volume of cartilage loss in a region of a cartilage defect of a cartilage in a joint of a mammal which method comprises determining the thickness, D_N, of the normal cartilage near the cartilage defect; obtaining the thickness of the cartilage defect, D_D, of the region; subtracting D_D from D_N to give the thickness of the cartilage loss, D_L; and multiplying the D_L value times the area of the cartilage defect, A_D, to give the volume of cartilage loss; (4) a method of estimating the change of cartilage in a joint of a mammal over time, which method comprises estimating the thickness or width or area or volume of a region of

A

cartilage at an initial time T_1; estimating the thickness or width or area or volume of the region of cartilage at a later time T_2; and determining the change in the thickness or width or area or volume of the region of cartilage between the initial and the later times; (5) a method for providing a biochemically based map of joint cartilage of a mammal, wherein the joint comprises cartilage and associated bones on either side of the joint, which method comprises measuring a detectable biochemical component selected from the group consisting of water, sodium and hyaluronic acid (Is this amendment necessary, since the biochemical components are mapped in 3D (see 2 lines down) and Paul does not teach 3D?throughout the cartilage; determining the relative amounts of the biochemical component throughout the cartilage; mapping the amounts of the biochemical component in three dimensions through the cartilage; and determining the areas of abnormally joint cartilage by identifying the areas having altered amounts of the biochemical component present; (6) a method of estimating the change of cartilage in a joint, wherein the joint comprises articular cartilage, which method comprises defining a 3D object coordinate system of the joint at an initial time, T_1; identifying a region of a cartilage defect within the 3D object coordinate system; defining a volume of interest around the region of the cartilage defect whereby the volume of interest is larger than the region of cartilage defect, but does not encompass the entire articular cartilage; defining the 3D object coordinate system of the joint at a second timepoint, T_2; placing the identically-sized volume of interest into the 3D object coordinate system at timepoint T_2 using the object coordinates of the volume of interest at timepoint T_1; and measuring any differences in cartilage volume within the volume of interest between timepoints T_1 and T_2; and (7) a method for correlating cartilage image data, bone image data, and optoelectrical image data for the assessment of the condition of a joint, which method comprises (a) obtaining the cartilage image data of the joint with a set of skin reference markers placed externally near the joint; (b) obtaining the bone image data of the joint with a set of skin reference markers positioned in the same manner as the markers in (a); (c) obtaining the optoelectrical image data of the joint with a set of skin reference markers positioned in the same manner as (a) and (b); and using the skin reference markers to correlate the images obtained in (a), (b) and (c) with each other, wherein each skin reference marker is detectable in the cartilage and bone data and the opto-electrical data.

3. The method of claim 1, wherein said electronic image provides information on the thickness, shape, or curvature of said normal and said disease tissue or the location and size of said diseased tissue.

4. The method of claim 1, wherein said therapy comprises autologous chondrocyte transplantation, osteochondral allografting, osteochondral autografting, tibial corticotomy, femoral or tibial osteotomy.

5. The method of claim 1, wherein said therapy uses cartilage or bone tissue grown ex vivo, stem cells, an artificial non-human material, an agent that stimulates repair of said diseased tissue, or an agent that protects said diseased tissue and that protects adjacent normal tissue.

6. The method of claim 1, wherein said information is used to determine the thickness or other geometrical feature of a tissue transplant, a tissue graft, a tissue implant, a tissue replacement material, a tissue scaffold, or a tissue regenerating material or tissue repair system.

7. The method of claim 1, wherein said image is obtained using ultrasound, computed tomography, positron emission tomography, a single photon emission computed tomography scan, or MRI.

8. The method of claim 7, wherein said information is used to generate a three-dimensional map of cartilage thickness or a physical model of said normal or said diseased tissue or both.

9. The method of claim 8, wherein said physical model is used to shape a tissue transplant, a tissue graft, a tissue implant, a tissue replacement material, a tissue scaffold or a tissue regenerating material or tissue repair system.

10. (Amended) A method of treating cartilage degeneration in a joint, which method comprises:

obtaining an electronic image of said joint, wherein said image includes both normal and diseased cartilage tissue;

electronically evaluating said image to obtain information selected from the group consisting of volume, area, thickness, geometry, water content, sodium content, hyaluronic acid or relaxation time of said normal or diseased tissue; and

selecting a therapy to treat or replace said degenerated cartilage, wherein said information is used during selection of treatment or replacement therapy of said degenerated cartilage.

11. The method of claim 10, wherein said information includes thickness, shape, curvature, or location and dimensions of said normal or degenerated cartilage.

12. The method of claim 10, wherein said technique to treat or replace said degenerated cartilage is autologous chondrocyte transplantation, osteochondral allografting, osteochondral autografting, tibial corticotomy, or femoral or tibial osteotomy.

13. The method of claim 10, wherein said treatment or replacement therapy uses cartilage or bone tissue grown ex vivo, stem cells, an artificial non-human material, an agent that stimulates repair of said diseased tissue, or an agent that protects said diseased tissue and that protects adjacent normal tissue.

14. The method of claim 10, wherein said information is used to determine the thickness, shape, curvature, or location and dimensions of a cartilage transplant, a cartilage graft, a cartilage implant, a cartilage replacement material, a scaffold for cartilage cell or acellular cartilage components or a cartilage regenerating material or a cartilage repair system.

15. The method of claim 10, wherein said image is obtained using ultrasound, computed tomography, positron emission tomography, a single photon emission computed tomography scan, or MRI.

16. The method of claim 10, wherein said information is used to generate a three dimensional map of cartilage thickness or a physical model of said normal or said diseased tissue or both.

17. The method of claim 16, wherein said physical model is used to shape a cartilage transplant, a cartilage graft, a cartilage implant, a cartilage replacement material, a scaffold or a cartilage regenerating material or a cartilage repair system.

18. The method of claim 16, wherein physical model comprises an area of diseased cartilage as well as adjacent normal tissue.

19. The method of claim 18, wherein said adjacent normal tissue is bone, bone marrow, or normal cartilage.

20. The method of claim 16, wherein said physical model is created with use of a 3D Euclidian distance transformation.

21. The method of claim 16, wherein said physical model or a portion of said physical model is implanted into a knee joint.

22. The method of claim 16, wherein said physical model carries cartilage cells or cartilage matrix.

23. A method of treating a human with diseased cartilage in a joint, which method comprises: utilizing an MRI scan to generate a cross-sectional electronic image of said joint, wherein said image includes both normal and diseased cartilage; and utilizing information from said image to create a geometric model of an area of diseased cartilage, wherein said geometric model is used in selecting a treatment of said diseased cartilage.

24. The method of claim 23, wherein said area of diseased cartilage includes adjacent normal tissue.

25. The method of claim 23, wherein said geometric model is used to determine the shape of a cartilage transplant, a cartilage graft, a cartilage implant, a cartilage replacement material, a scaffold for cartilage cells or acellular cartilage components or a cartilage regenerating material or a cartilage repair system.

26. A method of assessing cartilage disease in a joint, wherein the joint comprises cartilage and accompanying bones on either side of the joint, which method comprises: obtaining a three-dimensional map of the cartilage demonstrating the thickness or biochemical contents or relaxation time of normal and diseased cartilage; and determining the margins of the diseased cartilage in relationship to the normal cartilage in said three-dimensional map.

27. The method of claim 26, wherein said determination of said margins of said diseased cartilage is performed by detecting a difference in said thickness, said biochemical contents or said relaxation time between said normal and said diseased cartilage.

28. The method of claim 26, wherein said determination of said margins of said diseased cartilage is used to determine the area, volume, or thickness of diseased cartilage.

29. The method of claim 26, wherein said determination of said margins of said diseased cartilage is used to determine the percentage of total cartilage surface area in a joint or along an articular surface represented by diseased cartilage or the percentage of weight-bearing surface area in a joint represented by diseased cartilage.

30. The method of claim 26, wherein steps (a) through (b) are carried out at an initial time (T_1) and are carried out again at a later time (T_2).

31. The method of claim 30, wherein the estimation includes an analysis of the degree of degeneration of the cartilage between T_1, and T_2.

32. The method of claim 26, wherein an MRI technique first obtains a series of two-dimensional views of the joint, which are then mathematically integrated to give a three dimensional image.

33. The method of claim 32, wherein the MRI technique employs a gradient echo, spin echo, fast-spin echo, driven equilibrium Fourier transform, or spoiled gradient echo technique.